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BALASUBRAMANIAN, VENKATARAMAN	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/696,862
Filing Date: October 30, 2003
Appellant(s): CAO ET AL.

Daniel A. Pearson
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 08/03/2009 appealing from the Office action mailed 04/16/2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

JP 2002053566 (English Machine Translation) Inaba 02-2002

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 5, 8-12, 14-20, 23-29, 31, 33-46 and 54-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inaba et al., JP 2002053566 (English Machine Translation relied on.)

Inaba et al., teaches several thiazole compounds of formula I as kinase inhibitors useful for treating various diseases including Alzheimer's disease and allergy, which includes se of instant compounds. See page 1, formula I and note with the given definition of various variable groups, the compounds taught include instant compounds, though excluded by the proviso. See entire document, especially Table shown in pages 23-99. Particularly see compounds 44, 51, 80 and 113.

Instant compounds permit the pyridine ring and the amide side chain to be at various available positions in the thiazole ring.

While said compound(s) doesn't anticipate the scope of instant claims in view of the proviso in claim 1, they are very closely related, being positional isomers of compounds i.e. 2-carbamido and 5-pyrido of instant vs. 2-carbamido and 4-pyrido in the thiazole ring of the reference.

However, positional isomers are not deemed patentably distinct absent evidence of superior or unexpected properties. See In re Crounse, 150 USPQ 554; In re Norris 84 USPQ 458; In re Finely 81 USPQ 383 and 387; Ex parte Engelhardt, 208 USPQ 343; Ex parte Henkel, 130 USPQ 474, regarding positional isomers.

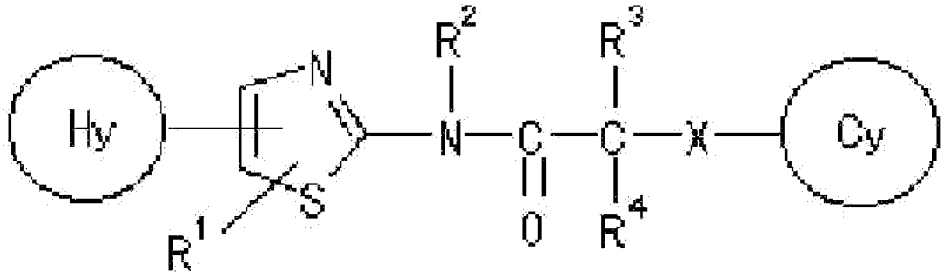
Thus it would have been obvious to one skilled in the art at the time of the invention was made to expect instant compounds to possess the utility taught by the applied art in view of the close structural similarity outlined above.

(10) Response to Argument

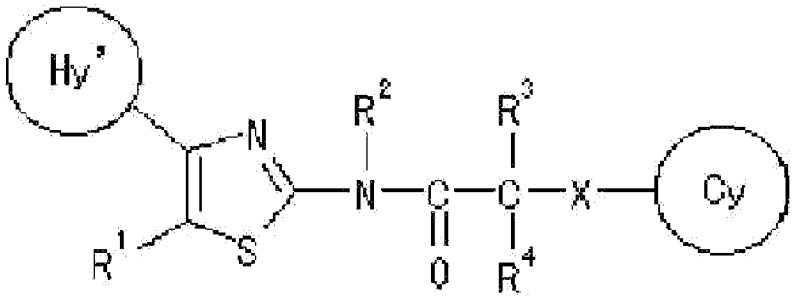
Appellants' traversal is not persuasive.

Appellants have not fully considered the factual basis for the above 103 rejection.

Inaba teaches compound of formula I and its subgenus compound of formula II.

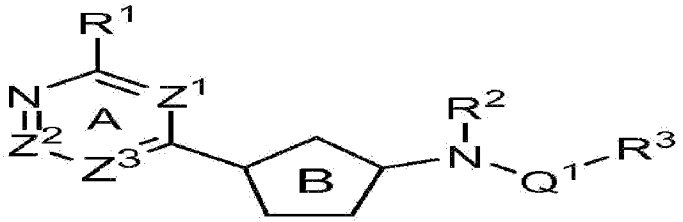


[I]



[II]

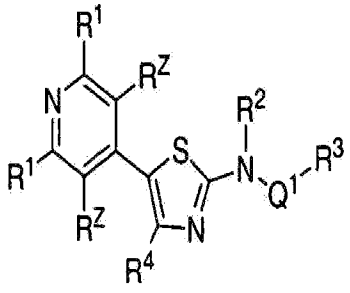
When Hy or Hy' is 4-pyridyl group, with the given definition of various variable groups, the compound of formula I and its subgenus compound of formula II include generically include appellants genus of compound of formula I when B ring choice is second choice and fifth choice. Structural formula of appellants' compound of formula I is:

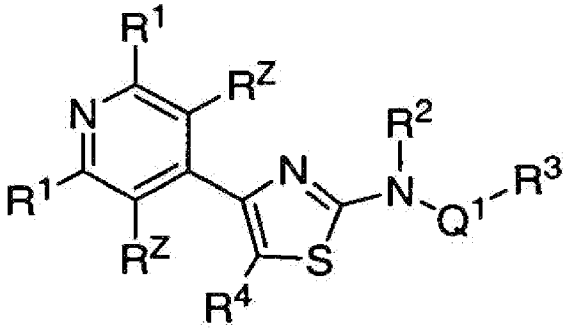


I

The specific compounds of appellants with the above two B choices, which are taught in Inaba, are of formula IV-E shown in page 35 and formula VII-A of the specification shown below:

IV-E



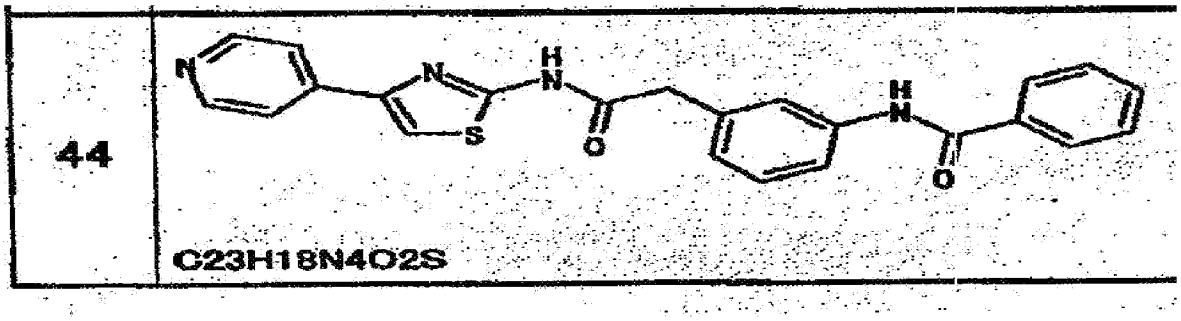


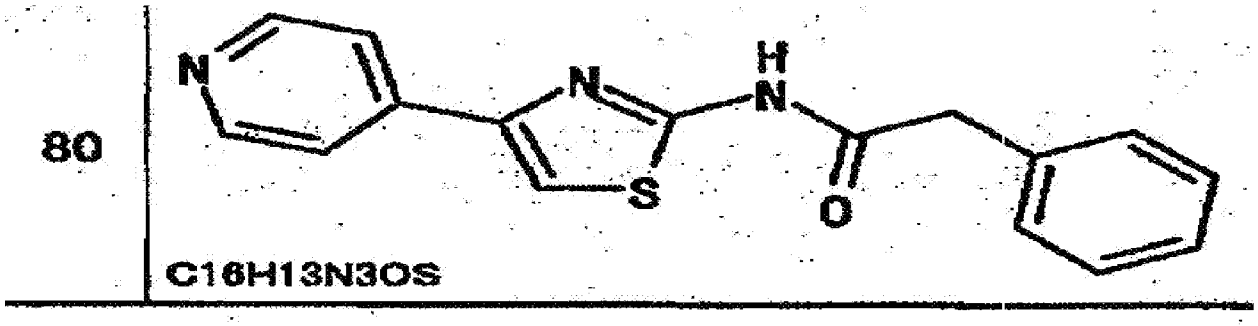
VII-A

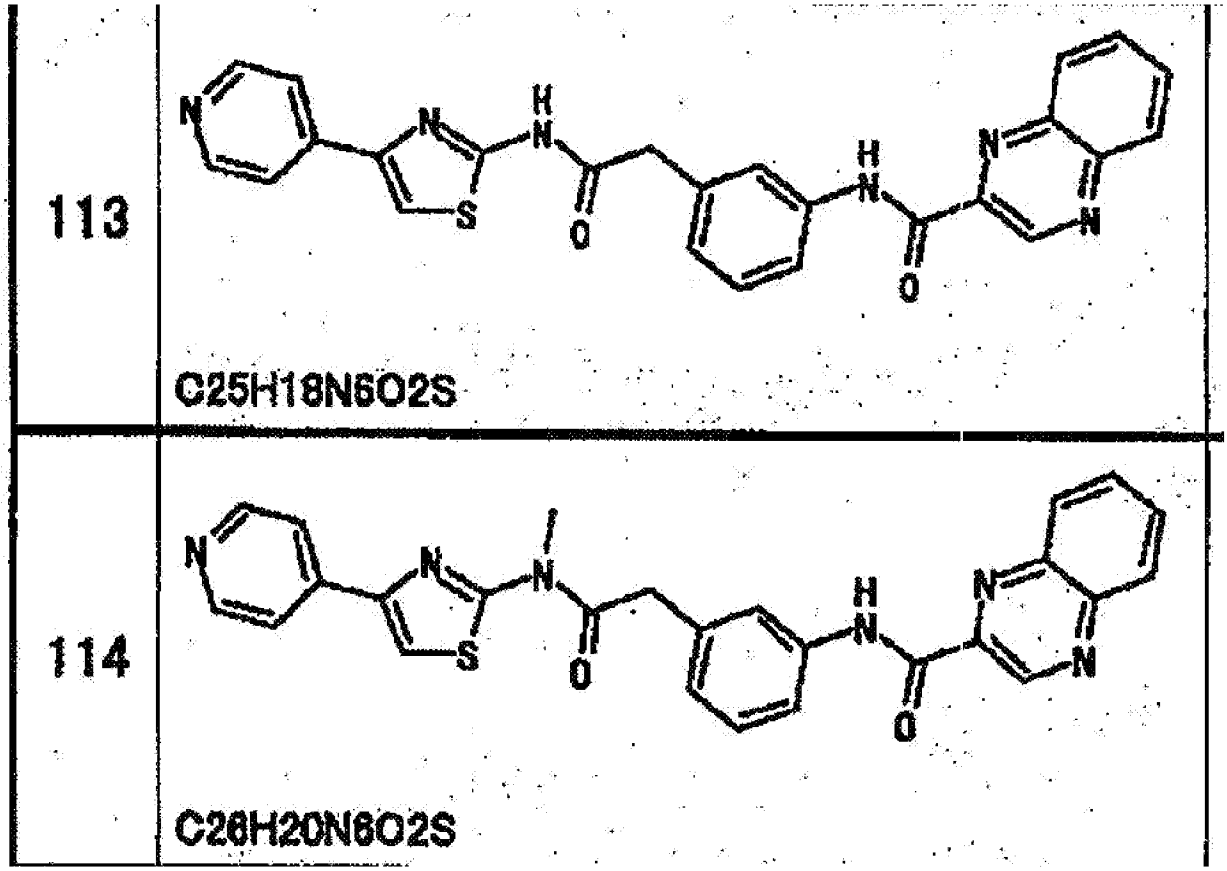
As noted above, Inaba teaches but appellants have excluded thes generically teaches the instant genus. Note with given choices of R', Inaba's genus

include instant genus. In addition, appellants claim the positional isomer of these compounds with B ring choice 5, formula IV-E.

Exemplified compounds of Inaba:







More specifically, Inaba teaches thiazole compounds wherein the 4-pyridyl group is attached to the 4-position of the thiazole while appellants claim thiazole compounds wherein the 4-pyridyl is attached to the 5-position of the thiazole as shown above.

Thus, only difference between Inaba's thiazole and appellants' thiazole is the position 4-pyridyl. Clearly appellants are claiming the positional isomer of compound taught by Inaba. Positional isomers are obvious variant. It would be obvious to one trained in the art to switch the position of attachment of 4-pyridyl from 4 to 5 position of thiazole and expect these compounds have the same use taught for the compound with 4-pyridyl in 4-positon of thiazole.

It is well established that position isomers are prima facie structurally obvious even in the absence of a teaching to modify. The isomer is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers. This circumstance has arisen many times. See: Ex parte Englehardt, 208 USPQ 343, 349; In re Mehta, 146 USPQ 284, 287; In re Surrey, 138 USPQ 67; Ex parte Ullyot, 103 USPQ 185; In re Norris, 84 USPQ 459; Ex parte Naito, 168 USPQ 437, 439; Ex parte Allais, 152 USPQ 66; In re Wilder, 166 USPQ 545, 548; Ex parte Henkel, 130 USPQ 474; Ex parte Biel, 124 USPQ 109; In re Petrzilka, 165 USPQ 327; In re Crownse, 150 USPQ 554; In re Fouche, 169 USPQ 431; Ex parte Ruddy, 121 USPQ 427; In re Wiechert, 152 USPQ 247, In re Sherry, 195 USPQ 753; In re Jones, 74 USPQ 152, 154.

For example, "Position isomerism has been used as a tool to obtain new and useful drugs" (Englehardt) and "Position isomerism is a fact of close structural similarity" (Mehta, emphasis in the original);

Note also In re Jones, 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to prima facie obviousness"; one of those listed is "adjacent homologues and structural isomers". Position isomers are the basic form of close "structural isomers."

Similar is In re Schechter and LaForge, 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds."

Note also In re Deuel 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds.., a known compound may suggest its analogs or isomers, either geometric isomers (cis v. trans) or position isomers (e.g., ortho v. para)." See also MPEP 2144.09, second paragraph.

Appellants have argued that the compounds exemplified by Inaba are only 2 % and that it is small genus of compounds and does not reflective of Inaba reference as whole. This argument is also not persuasive. Contrary to appellants' assertion, the compounds taught by Inaba represent the genus of thiazole compounds taught and claimed by Inaba. There is no requirement that entire genus of thiazole compounds of Inaba should be enabled. Representative examples are enough to provide guidance for objective enablement of the entire genus. Inaba teaches over 306 thiazole compounds including those having 4-pyridyl side chain and provides adequate guidance to make these compounds as seen in pages 20-30.

Furthermore, appellants are applying a different standard to genus of Inaba as compared to their genus. Even by a rough estimate, appellants' genus embraces millions of compounds and a careful estimate may exceed billion compounds. Of which, instant specification exemplifies 457 compounds. Appellants apparently urging these 457 compounds represent the whole genus of millions, if not billions, of compounds claimed by the appellants. If such is the case, then based on appellants' urging, by applying same standard of analysis, exemplified 306 compounds of Inaba truly represent whole genus taught and claimed by Inaba. In addition, appellants exemplify

only 346 compounds (I-B1-346) which are compounds with 4-pyridyl substituents on 5-positon of the thiazole and appellants have not exemplified a single thiazole compound with 4-pyridyl substituted at the 4-position of the thiazole. Yet appellants claim 4-pyridyl substituted at the 4-position of the thiazole generically and expects that exemplified compounds as representative for the thiazole compound with 4-pyridyl substituted at the 4-position of the thiazole. Hence, if one were to grant exemplified compounds of appellants truly represent the genus as whole then such should be granted for exemplified compounds of Inaba to be reflective of whole genus.

Appellants have also argued that 90% of the 246 Inaba compounds tested showed more PKC activity than Inaba compound 44, and that compound 51 and 80 were not tested and therefore, the biological activity of pyridinyl thiazole compounds indicate they are inferior kinase inhibitors compared to majority of compounds described therein and hence the reference teaches away from pyridinyl thiazoles. This argument is also not found persuasive.

Appellants' assessment of the biological data is not entirely correct and accurate. As seen in pages 185-196, Inaba has tested 246 compounds as stated by the appellants. Appellants' assessment of inferior compounds appear to be based on bias than factual basis as there is no clear-cut definition of what is inferior and there is nothing in Inaba reference which indicates or states the pyridinyl thiazoles are not suitable for the use taught therein that would deter one away from making this compounds. The biological activity shown in pages 185-196 are activity among three isoforms of PKC and most them far fall below <1μM for at least one isoform and on the

whole are well below 5μM. One trained in the art would consider these compounds to be active and expect them to be useful for treating diseases taught therein. One would expect relative variation in activity among compounds of genus and among isoforms of enzymes.

This is also clear from appellants' specification. Specification does not show any detailed biological activity data but relies on paragraph [00296] of page 153, which states "Compounds of the invention were found to inhibit PKA. In certain embodiments, compounds were shown to have a Ki of less than 1μM for PKA". Based on this, it may be surmised that appellants have not tested all compounds made and that some of them have less than Ki of less than 1μM for PKA. Hence, what appellants considers as inferior inhibitors is not clearly defined and that there is no reason to believe compounds that show activity 5μM or below 5μM to be inferior inhibitors. Again, it should be emphasized that appellants have not made a single pyridinyl thiazole compound with 4-pyridinyl group in 4-position of thiazole and hence appellants cannot assert that these compounds are superior to Inaba's compounds.

Furthermore, Inaba compound 44, contrary to appellants assessment, has activity less than <1μM for isoforms of PKC (β and ϒ) and Inaba compound 113 has <1μM among all three isoforms tested as shown in page 186 and 189.

Hence, Inaba's pyridinyl thiazole compounds are clearly active as PKC inhibitors and one trained in the art would be motivated to make them and their positional isomers stated above as he would expect them to have the use taught therein.

As noted in the previous office action, Inaba anticipated the method of use claims 54-57 before the current amendment.

Appellants have argued that that Inaba did not teach treating Alzheimer's diseases and allergy embraced in the instant claims but taught use of the compounds as sedative. This is not correct.

Inaba teaches his thiazole compounds are PKC inhibitors and that PKC inhibitors are useful for treating a number diseases including Alzheimer's disease, diabetes, diabetic complications such as retinopathy. See English Machine Translation of Inaba provided on 04/16/2008. For example, in paragraph 0002 (pages 1-2) paragraph 0026 (page 10) and paragraph 0180 (page 124-125), Inaba teaches use of PKC inhibitors for treating diseases including diabetes, diabetic complications such as retinopathy, and Alzheimer's disease. See also page 4, second paragraph wherein use of related compound for treating asthma and allergy.

Furthermore, Appellants have not shown any unexpected or superior results with the instant genus of compounds. Inaba et al., clearly teaches instant genus and the compounds of Inaba include positional isomers of instant genus. Thus, one trained in the art would be motivated to make compounds of Inaba including the positional isomers and expect those compounds to have use taught therein. See In re KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727 (2007), wherein the court stated that

[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads

to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Such is the case with instant claims. Shifting the position of 4-pyridyl group from 5-position taught in the reference to 4-position is a finite choice and obvious variant. One trained in the art would be motivated to make such positional isomers for the use taught in the reference.

Based on these considerations, this rejection is proper and is maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Venkataraman Balasubramanian/

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